STIC-ILL

QP 357.S56716

From: Li, Janice
Sent: Monday, May 05, 2003 3:02 PM
To: STIC-ILL
Subject: 10023335

Please provide the following:

TI Ethopharmacology of imipramine in the forced-swimming test: gender differences
AU Barros H M T (Reprint); Ferigolo M
SO NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS, (DEC 1998) Vol. 23, No. 2, pp. 279-286.

TI Strain Differences in the Behavioral Effects of Antidepressant Drugs in the Rat Forced Swimming Test
AU Lopez-Rubalcava, C.; Lucki, I.
SO Neuropsychopharmacology (1999), Volume Date 2000, 22(2), 191-199.

TI Open field, learned helplessness, conditioned defensive burying, and forced-swim tests in WKY rats.
AU Pare W P
SO PHYSIOLOGY AND BEHAVIOR, (1994 Mar) 55 (3) 433-9.

TI Differences in the stress response of Wistar-Kyoto (WKY) rats from different vendors.
AU Pare W P; Kluczynski J
CS V. A. Medical Center, Perry Point, MD 21902-1040, USA.. wpare@aol.com
SO PHYSIOLOGY AND BEHAVIOR, (1997 Sep) 62 (3) 643-8.

TI Behavioural profiles of two Wistar rat lines selectively bred for high or low anxiety-related behaviour
AU Liebsch G; Montkowski A; Holsboer F; Landgraf R (Reprint)
SO BEHAVIOURAL BRAIN RESEARCH, (AUG 1998) Vol. 94, No. 2, pp. 301-310.

TI A biobehavioral profile of an ulcer susceptible rat strain
AU Pare, William P.; Redei, Eva
CS Eastern Research and Development Office, VA Medical Center, Perry Point, MD, 21902, USA
SO Hans Selye Symposia on Neuroendocrinology and Stress (1995), 2(Neuroendocrinology of Gastrointestinal Ulceration), 201-8

TI Characterization of Wistar Kyoto (WKY) rat sub-strains selectively bred for depressive-like behavior in the forced swim test.
AU Solberg, L. C. (1); Will, C.; Turek, F. W. (1); Redei, E.
SO Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 849. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience

Q. Janice Li, M.D.
Patent Examiner, AU1632
CM1, Rm11A17
Mail Box 12E12
703-308-7942

341.3

PHENOTYPIC DEFICITS IN GFAP-IL6 TRANSGENIC MICE. L.H. Gold,* I.L. Campbell, J. McDonald, L. H. Parsons, S. Henry and V. David. Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA 92037.

The cytokine interleukin-6 (IL6) has been found to be expressed in the central nervous system (CNS) associated with a chronic inflammatory state observed in several neurodegenerative diseases such as Alzheimer and infectious diseases including HIV dementia complex. The relationship between the CNS expression of IL6, inflammatory neurodegeneration and clinical behavioral pathology is currently under investigation. Mice that express IL-6 chronically in astrocytes exhibit a well characterized neuropathology, associated with cognitive deficits (Heyser et al., 1997). We report here a series of experiments further assessing the behavioral phenotypes in male and female GFAP-IL6 +/+ +/- and -/- transgenic mice. Similar sensitivities to the effects of drugs of abuse were observed in control and transgenic mice tested for cocaine- and heroin-induced locomotor activity. Interestingly, Consistent with their previously reported blood brain barrier leakage, transgenic mice had increased cocaine levels in brain determined 30 min after injection. Longitudinal assessment of coordinated motor performance using a rotating rod revealed an age- and transgene-dose dependent impairment. Procedural/associative learning and cognitive flexibility were evaluated using successive and simultaneous spatial discrimination in a Y maze, followed by reversal. Whereas reference memory in the associative tasks is mostly spared by age or IL-6 overexpression, cognitive adaptability is sensitive to both, with a different pattern in males and females. Finally, others have shown IL6 to be important in the reduction in sucrose preference observed in an autoimmune mouse model (Sakic et al., 1997). Thus, sucrose preference is being examined in the GFAP-IL6 transgenic mice. These studies will further elucidate the role of IL6 in behavioral pathogenesis associated with a variety of neurodegenerative, neuroinflammatory and infectious diseases. Supported by PHS grants DA10191, MH47680 and MH50426.

341.4

ACUTE INHIBITION OF THE NEURONAL NITRIC OXIDE SYNTHASE INCREASES NON SELECTIVE ATTENTION IN THE NAPLES HIGH EXCITABILITY RAT.

A.Fresiello , G. De Filippis and A.G. Sadile. (SPON: INTERNATIONAL BEHAVIOR & GENETICS SOCIETY) Lab. Neurophysiol. Behav. & Neural Networks, Med. Sch., II Univ. Naples, Italy.

The involvement of nitric oxide (NO) in the process of non-selective attention (NSA) towards environmental stimuli has been investigated in a putative animal model of Hyperactivity and Attention Deficits, the Naples High-Excitability rat (NHE). To this aim, the frequency and duration of rearing episodes in a novelty situation has been measured, following acute inhibition of the neuronal isoform of the enzyme nitric oxide synthase (n-NOS) by the non competitive inhibitor 7-Nitroindazole (7-NINA). Adult male NHE rats received a single intraperitoneal injection of 7-NINA (0.1-10 mg/kg) or vehicle 30 min. before testing on day 1. Rats were exposed to a Lât- maze on three consecutive days for a 10-min. period at 24-h interval. The results showed that all doses of 7-NINA were effective in determining a 2-fold increase in the duration of rearing episodes, compared to vehicle controls. In contrast, the drug exerted a dose dependent reduction in the frequency of both horizontal and vertical activity. Thus, these findings obtained by selective inhibition of n-NOS by an allosteric inhibitor that increases arginine availability without displacing the inhibitor from n-NOS, strengthen the hypothesized role of NO in NSA. (Supported by Telethon-Italy grant E.513).

341.5

ENVIROMENTAL FACTORS DURING POST NATAL PERIOD SIGNIFICANTLY MODIFY NON SELECTIVE ATTENTION AND ACTIVITY IN THE NAPLES HIGH EXCITABILITY RAT.

G. De Filippis , A.Fresiello and A.G. Sadile. (SPON: EUROPEAN BRAIN AND BEHAVIOUR SOCIETY). Lab. Neurophysiol. Behav. & Neural Networks, Med. Sch., II Univ. Naples, Italy.

The involvement of epigenetic factors in the development of brain systems and the phenotypic expression of the neural systems underlying attentive processes has been investigated in an animal model of hyperactivity and attention deficits, the Naples High Excitability rat (NHE). To this aim, male NHE pups have been reared in small (4) or normal litter size (9) during the first four weeks of postnatal life. Both groups underwent a differential handling procedure occurring 1, 2, or 4 times a week. At the end of the fourth week, rats were weaned and housed in groups of 2 and tested as young adults for non selective attention in a spatial novelty situation for three consecutive tests at 24h intervals. The behavior was videotaped and analyzed off line for the frequency and duration of corner crossings and rearings. The results indicate that the increased maternal care and high fat diet induced by the small litter size produced long lasting effects on the duration of rearing episodes that indexes non selective attention. Moreover, differential handling exerted a complex effect that was beneficial at low stimulation level only. Thus, these findings suggest that epigenetic factors acting during critical periods of post-natal development may interact with genetic determinants that in turn influence the maturation of the neural systems controlling attentive processes. (Supported by Telethon-Italy grant E.513).

341.6

CHARACTERIZATION OF WISTAR KYOTO (WKY) RAT SUB-STRAINS SELECTIVELY BRED FOR DEPRESSIVE-LIKE BEHAVIOR IN THE FORCED SWIM TEST. L.C. Solberg*[1,2], C. Will[2], F.W. Turek[1], and E. Redei[2]. [1]Dept. of Neurobiology and Physiology; [2]Dept. of Psychiatry and Behavioral Sciences, Northwestern University, Chicago, IL, 60611.

The Wistar Kyoto (WKY) rat shows depressive-like behavior, as well as alterations in the diurnal rhythms of the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) hormones. However, in addition to a large variation in the behavioral and hormonal measures, DNA fingerprinting studies have shown that the WKY is not truly inbred. To create a truly genetic model, we have selectively bred the WKY rat, using immobility in the Forced Swim Test (FST) as a functional selector. We mated WKY's with the highest and lowest immobility in the FST, resulting in WKY-most depressed (WMD) and WKY-least depressed (WLD) sub-strains. We continued brother-sister in-breeding in subsequent generations, choosing founder litters with the highest and lowest immobility, for WMD and WLD, respectively. WMD parents, F1 and F2's exhibit increased immobility in the FST relative to WLD parents, F1 and F2's. We have also measured behavior in the Open Field Test (OFT), as well as HPA and HPT diurnal hormone levels in the F1 generation. WMD F1's show decreased locomotion in the OFT relative to WLD F1's. However, no significant differences in HPA or HPT hormone levels are found between F1 WMD and WLD's. This finding is in contrast to the diurnal hormonal rhythm differences seen between WKY and non-depressed Wistar rats. The separation of behavioral and hormonal phenotypes in the selectively bred sub-strains suggests that there is no simple, direct relationship between HPA and HPT hormones and the depressive-like behavior in this animal model. We are continuing to in-breed the WMD and WLD sub-strains to investigate the genetic basis for the depressive-like behavior in the WKY. This work was supported by [1]the National Award for Research on Schizophrenia and Depression, NIH HL/MH-96015 and the [2]Berman Foundation.

341.7

DIFFERENTIAL DISPLAY FROM AMYGDALA OF AN ANIMAL MODEL OF ENDOGENOUS DEPRESSION. C. Will,[1] F. Aird[1]*, [1] L. Solberg, [1,2] E Redei.[1] [1]Dept. of Psychiatry and Behavioral Sciences, Northwestern Univ. Med. Sch.; [2]Dept. of Neurobiology and Physiology, Northwestern Univ.; Chicago, IL 60611.

The Wistar Kyoto rat (WKY) is an ideal model of depression in which to study the molecular mechanisms of this illness since WKY demonstrates endogenous behavioral and hormonal abnormalities that mimic those found in some symptom presenting depressive patients. There is evidence suggesting that WKY is not truly inbred. Therefore, we have selectively bred WKY (Harlan Prod. for Biosci., Inc.) for depressive behavior using immobility in the forced swim test (FST) as a functional selector. Breeding for high and low immobility in the FST resulted in 2 sub-strains, WKY 'most depressed' (WMD) and WKY 'least depressed' (WLD).

Recently, functional imaging studies found increased metabolic activity in the amygdala of depressed patients compared to normal controls independent of disease status. This increased metabolic activity could result in differential expression of specific genes in predisposed individuals. Therefore, analyzing the gene expression in the amygdala of selectively bred WKY may produce candidate genes involved in the trait of depression.

Differential Display (DD) was used previously to compare gene expression in the amygdala of WKY and Wistar (Wi) rats. A three-primer pair comparison resulted in 37 differentially expressed bands. Comparison of amygdala RNA of the parental generation mothers for the two sub-strains using the same primer pairs resulted in 10 differentially displayed bands, indicating that indeed there is differential gene expression in the amygdala in the WMD and WLD parental generations. Differences in amygdala gene expression in subsequent generations of WMD and WLD are hypothesized to be directly related to differences in depressive behavior in these sub-strains. This research was supported by The Berman Foundation.

341.8

SPONTANEOUS STEREOTYPY IN AN ANIMAL MODEL OF DOWN SYNDROME (TS65DN MICE). M.H. Lewis[1], S.B. Powell[1], C.A. Turner[1], H.A. Newman[1], P. Bugenhagen[1], P. Gendreau[1]*, L. Crnic[2]. [1]Departments of Psychiatry & Psychology, University of Florida, Gainesville, FL 32610; [2]Departments of Psychiatry & Pediatrics, University of Colorado School of Medicine, Denver, CO 80262.

Stereotyped behaviors (e.g., body rocking) occur at high rates in individuals with mental retardation (e.g., Down syndrome). To determine if spontaneous stereotypy occurs in an animal model of Down syndrome (Ts65Dn), we videotaped Ts65Dn and control mice left undisturbed in their home cages for 5 hours/day on two consecutive days during their dark cycle. Additional measures of motor behavior following a mild environmental challenge (i.e., novelty), were collected using an activity monitor. In home cage observations, 3 of 9 (33%) Ts65Dn mice displayed stereotyped jumping (up to 41% of time observed) with an additional 3 animals (33%) displaying cagetop twirling (20% of time), for a total of 67% exhibiting stereotypy. None of the control mice exhibited jumping and 9% (1/11) engaged in cagetop twirling (35%). Ts65Dn and control mice did not differ in locomotor activity in either the home cage or the activity monitors. In independent observations trisomic mice exhibited stereotyped jumping during stressful testing (8/10 trisomics and 2/10 controls in shock motivated discrimination; 6/10 trisomics and 0/10 controls during rotorod testing). The current model may provide a useful tool to begin to assess the genetic basis of stereotyped behavior in humans. Supported by MH56163, HD04024 and HD17449.